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=> d stat que l7

L1            1 SEA FILE=REGISTRY ATENOLOL/CN
L3              SEL  L1 1- CHEM :      10 TERMS
L4         3108 SEA FILE=HCAPLUS L3
L5         3108 SEA FILE=HCAPLUS L4 OR ATENOLOL
L6          491 SEA FILE=HCAPLUS L5 AND (CARDIOVASCUL? OR HEART(W)(DISEASE? OR
                DISORDER?) OR THROMBOSIS OR ANGINA OR DYSRHYTHMIA)
L7            8 SEA FILE=HCAPLUS L6 AND ?SURG?


=> d l7 ibib abs hitrn


L7   ANSWER 1 OF 8  HCAPLUS  COPYRIGHT 2000 ACS
ACCESSION NUMBER:         2000:29632  HCAPLUS
DOCUMENT NUMBER:          132:59091
TITLE:                    Beneficial effects from .beta.-adrenergic blockade in
                          elderly patients undergoing noncardiac surgery
AUTHOR(S):                Zaugg, Michael; Tagliente, Thomas; Lucchinetti,
                          Eliana; Jacobs, Ellis; Krol, Marina; Bodian, Carol;
                          Reich, David L.; Silverstein, Jeffrey H.
CORPORATE SOURCE:         Departments of Anesthesiology, Surgery, Geriatrics and
                          Adult Development, Pathology and Biomathematical
                          Sciences, The Mount Sinai School of Medicine, New
                          York, NY, 10029-6574, USA
SOURCE:                   Anesthesiology (1999), 91(6), 1674-1686
                          CODEN: ANESAV; ISSN: 0003-3022
PUBLISHER:                Lippincott Williams & Wilkins
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Perioperative .beta.-blockade has been shown to improve long-term cardiac
```

outcome in noncardiac **surgical** patients. A possible mechanism for the reduced risk of perioperative myocardial infarction is the attenuation of the excitotoxic effects of catecholamine **surges** by .beta.-blockade. It was hypothesized that .beta.-blocker-induced alteration of the stress response was responsible for the reported improvements in **cardiovascular** outcome. Several variables assocd. with the perioperative use of .beta.-blockade were also evaluated. Sixty-three patients were randomly assigned to one of three groups: group I, no **atenolol**; group II, pre- and post-operative **atenolol**; group III, intraoperative **atenolol**. Hormonal markers of the stress response (neuropeptide Y, epinephrine, norepinephrine, cortisol, and adrenocorticotropic hormone) were evaluated preoperatively and for 72 h after **surgery**. Perioperative .beta.-blockade did not significantly alter the hormonal stress response. However, the .beta.-blocked patients showed improved hemodynamic stability during emergence and postoperatively. They also received less fentanyl intraoperatively (27.7%, $P < 0.0001$), experienced faster early recovery, had lower pain scores, and required less analgesia in the postanesthesia care unit. Cardiac troponin I release was detected in 8 of 19, 4 of 20, and 5 of 20 patients in groups I, II, and III, resp. (not significant). Three patients in group I had cardiac troponin I levels consistent with myocardial infarction. .beta.-Blockade does not reduce the neuroendocrine stress response, suggesting that this mechanism is not responsible for the previously reported improved **cardiovascular** outcome. However, it confers several advantages, including decreased analgesic requirements, faster recovery from anesthesia, and improved hemodynamic stability. The release of cardiac troponin I suggests the occurrence of peri-operative myocardial damage in this elderly population, which appears to be independent of the neuroendocrine stress response.

IT **29122-68-7**, **Atenolol**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(beneficial effects from .beta.-adrenergic blockade in elderly human patients undergoing noncardiac **surgery**)

=> d l7 ibib abs hitrn 2-8

L7 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:426508 HCAPLUS
DOCUMENT NUMBER: 129:184042
TITLE: Diuretic-based treatment and **cardiovascular** events in patients with mild renal dysfunction enrolled in the systolic hypertension in the elderly program
AUTHOR(S): Pahor, Marco; Shorr, Ronald I.; Somes, Grant W.; Cushman, William C.; Ferrucci, Luigi; Bailey, James E.; Elam, Janet T.; Applegate, William B.
CORPORATE SOURCE: Department of Preventive Medicine, College of Medicine, University of Tennessee, Memphis, USA
SOURCE: Arch. Intern. Med. (1998), 158(12), 1340-1345
CODEN: AIMDAP; ISSN: 0003-9926
PUBLISHER: American Medical Association
DOCUMENT TYPE: Journal

LANGUAGE: English

AB It is expected that the treatment of hypertension in patients with renal disease decreases the risk of **cardiovascular** events, but the evidence in these patients is lacking. This paper assessed the effect of diuretic-based treatment on **cardiovascular** events in patients with isolated systolic hypertension and renal dysfunction. A total of 4336 persons aged 60 yr and older with systolic blood pressures of 160 mm Hg and higher and diastolic blood pressures of less than 90 mm Hg were randomly assigned to receive either placebo or chlorthalidone (12.5-25.0 mg/d), with the addn. of **atenolol** (25-50 mg/d) or reserpine (0.05-0.10 mg/d) if needed, and obsd. for 5 yr. The risk of first-occurring **cardiovascular** events, including stroke, transient ischemic attack, myocardial infarction, heart failure, coronary artery bypass **surgery**, angioplasty, aneurysm, endarterectomy, sudden death, or rapid death, was stratified according to baseline serum creatinine levels (35.4-84.0, 84.1-101.6, 101.7-119.3, and 119.4-212.2 .mu.mol/L [0.4-0.9, 1.0-1.1, 1.2-1.3, and 1.4-2.4 mg/dL]). Systolic blood pressure redn. was not affected by baseline serum creatinine levels. Active treatment did not affect the risk of serum creatinine levels becoming elevated during follow-up. The risk of hypokalemia with active treatment decreased significantly with increasing baseline serum creatinine levels. In the 4 baseline serum creatinine groups, the relative risk (95% confidence interval) of **cardiovascular** events developing with active treatment was 0.73 (0.54-0.97), 0.63 (0.49-0.82), 0.62 (0.44-0.87), and 0.59 (0.38-0.91). The results were similar for the outcomes of stroke or coronary artery events and in analyses stratified by sex or age. Diuretic-based treatment of patients with isolated systolic hypertension prevents the development of **cardiovascular** events in older persons with mild renal dysfunction.

IT **29122-68-7**, **Atenolol**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diuretic-based treatment and **cardiovascular** events in elderly hypertensive humans with mild renal dysfunction)

L7 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:75120 HCAPLUS
DOCUMENT NUMBER: 128:200771
TITLE: Prophylactic **atenolol** reduces postoperative myocardial ischemia
AUTHOR(S): Wallace, Arthur; Layug, Beth; Tateo, Ida; Li, Juliet; Hollenberg, Milton; Browner, Warren; Miller, David; Mangano, Dennis T.
CORPORATE SOURCE: Departments of Anesthesia, Medicine, and Epidemiology and Biostatistics, San Francisco VA Medical Center, University of California, San Francisco, USA
SOURCE: Anesthesiology (1998), 88(1), 7-17
CODEN: ANESAV; ISSN: 0003-3022
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Perioperative myocardial ischemia occurs in 20-40% of patients at risk for cardiac complications and is assocd. with a ninefold increase in risk for perioperative cardiac death, myocardial infarction, or unstable **angina**, and a twofold long-term risk. Perioperative **atenolol** administration reduces the risk of death for as long as 2 yr after **surgery**. This randomized, placebo-controlled,

double-blinded trial tested the hypothesis that perioperative **atenolol** administration reduces the incidence and severity of perioperative myocardial ischemia, potentially explaining the obsd. redn. in the risk for death. Two-hundred patients with, or at risk for, coronary artery disease were randomized to two study groups (**atenolol** and placebo). Monitoring included a preoperative history and phys. examn. and daily assessment of any adverse events. Twelve-lead electrocardiog. (ECG), three-lead Holter ECG, and creatinine phosphokinase with myocardial banding (CPK with MB) data were collected 24 h before until 7 days after **surgery**. **Atenolol** (0, 5, or 10 mg) or placebo was administered i.v. before induction of anesthesia and every 12 h after operation until the patient could take oral medications. **Atenolol** (0, 50, or 100 mg) was administered orally once a day as specified by blood pressure and heart rate. During the postoperative period, the incidence of myocardial ischemia was significantly reduced in the **atenolol** group: days 0-2 (**atenolol**, 17 of 99 patients; placebo, 34 of 101 patients; P = 0.008) and days 0-7 (**atenolol**, 24 of 99 patients; placebo, 39 of 101 patients; P = 0.029). Patients with episodes of myocardial ischemia were more likely to die in the next 2 yr (P = 0.025). Perioperative administration of **atenolol** for 1 wk to patients at high risk for coronary artery disease significantly reduces the incidence of postoperative myocardial ischemia. Redns. in perioperative myocardial ischemia are assocd. with redns. in the risk for death at 2 yr.

IT **29122-68-7, Atenolol**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prophylactic **atenolol** reduces postoperative myocardial ischemia in humans)

L7 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:5673 HCAPLUS
DOCUMENT NUMBER: 126:42496
TITLE: Effect of **atenolol** on mortality and **cardiovascular** morbidity after noncardiac **surgery**
AUTHOR(S): Mangano, Dennis T.; Layug, Elizabeth L. Layug; Wallace, Arthur; Tateo, Ida
CORPORATE SOURCE: San Francisco Veterans Affairs Medical Center, University of California, San Francisco, CA, 94121, USA
SOURCE: N. Engl. J. Med. (1996), 335(23), 1713-1720
CODEN: NEJMAG; ISSN: 0028-4793
PUBLISHER: Massachusetts Medical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

12/5/96

AB Perioperative myocardial ischemia is the single most important potentially reversible risk factor for mortality and **cardiovascular** complications after noncardiac **surgery**. Although more than 1 million patents have such complications annually, there is no effective preventive therapy. The authors performed a randomized, double-blind, placebo-controlled trial to compare the effect of **atenolol** with that of a placebo on overall survival and **cardiovascular** morbidity in patients with or at risk for coronary artery disease who were undergoing non-cardiac **surgery**. **Atenolol** was given i.v. before and immediately after **surgery** and orally there-after

for the duration of hospitalization. Patients were followed over the subsequent two years. A total of 200 patients were enrolled. Ninety-nine were assigned to the **atenolol** group, and 101 to the placebo group. One hundred ninety-four patients survived to be discharged from the hospital, and 192 of these were followed for two years. Over-all mortality after discharge from the hospital was significantly lower among the **atenolol**-treated patients than among those who were given placebo over the six months following hospital discharge (0 vs. 8 %), over the first year (3 % vs. 14 %), and over two years (10 % vs. 21 %, P-0.019). The principal effect was a redn. in deaths from cardiac causes during the first six to eight months. Combined **cardiovascular** outcomes were similarly reduced among the **atenolol**-treated patients; event-free survival throughout the two-year study period was 68 % in the placebo group and 83 % in the **atenolol** group. In patients who have or are at risk for coronary artery disease who must undergo noncardiac **surgery**, treatment with **atenolol** during hospitalization can reduce mortality and the incidence of **cardiovascular** complications for as long as two years after **surgery**.

IT **29122-68-7, Atenolol**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of **atenolol** on mortality and **cardiovascular** morbidity after noncardiac **surgery** in humans)

L7 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:236960 HCAPLUS
DOCUMENT NUMBER: 125:982
TITLE: Total ischemic burden European trial (TIBET). Effects of ischemia and treatment with **atenolol**, nifedipine SR and their combination on outcome in patients with chronic stable **angina**
AUTHOR(S): Dargie, H. J.; Ford, I.; Foxt, K. M.
CORPORATE SOURCE: University Glasgow, Glasgow, G12 8QQ, UK
SOURCE: Eur. Heart J. (1996), 17(1), 104-12
CODEN: EHJODF; ISSN: 0195-668X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The relationship was studied between the presence or absence of ischemic events on Holter monitoring and occurrence of a hard or hard+soft endpoint. Hard endpoints were cardiac death, nonfatal myocardial infarction and unstable **angina**; soft endpoints were coronary artery bypass **surgery**, coronary angioplasty and treatment failure. The study showed no evidence of an assocn. between the presence, frequency or total duration of ischemic events on Holter monitoring, either on or off treatment, and the main outcome measures. There was a non-significant trend to a lower rate of hard endpoints in the group receiving combination therapy. Compliance, as measured by withdrawal from trial medication, was clearly poorest in the nifedipine group with similar withdrawal rates in the **atenolol** and combination therapy groups. The recording of ischemic events in 48 h Holter monitoring failed to predict hard or hard+soft endpoints in patients with chronic stable **angina**.

IT **29122-68-7, Atenolol**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(effects of ischemia and treatment with **atenolol**, nifedipine SR and their combination on outcome in patients with chronic stable **angina**)

L7 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:882604 HCAPLUS
DOCUMENT NUMBER: 123:329918
TITLE: Role of calcium channel blockers in diabetic renal transplant patients: preliminary observations on protection from sepsis
AUTHOR(S): Weinrauch, L. A.; D'Elia, J. A.; Gleason, R. E.; Shaffer, D.; Monaco, A. P.
CORPORATE SOURCE: Department of Medicine, Deaconess Hospital, Boston, MA, USA
SOURCE: Clin. Nephrol. (1995), Volume Date 1995, 44(3), 185-92
CODEN: CLNHBI; ISSN: 0301-0430
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Diabetic recipients of kidney transplants have an excessively high risk of allograft loss, infectious complications with sepsis, **cardiovascular** events and early death. This study was designed to det. whether post-transplantation medical management influenced long-term results. Seventy consecutive diabetic recipients of cadaveric renal allografts were followed from the time of transplant. Treatment regimens were based on the clin. judgment of transplant nephrologists and **surgeons**, not by the study team. Patients were followed for 2 to 9 yr (mean follow-up of 50.85 mo, one lost to follow-up). Groups were classified by HLA match, type of immunosuppression, prior **cardiovascular** history, type of antihypertensives (36 on calcium channel blockers, 32 on beta blockers, 8 ACE inhibitors). Events were defined as myocardial infarction, CVA, graft loss with return to dialysis, life-threatening sepsis, or death. Twenty allografts failed during the study, 24 patients died. Potentially cardioprotective drugs did not impact significantly on cardiac death, MI or CVA. Survivals were better when calcium channel blockers were used (mean 71.7 vs. 38.6 mo,; 4-yr survival 84 vs. 58%). When both beta and calcium channel blockers were used, patient mean survival was 72.5 mo vs. 36.8 mo for 21 patients who were not treated with blockers. There was a lower incidence of graft loss when beta blockers and calcium channel blockers were used: at mean patient survival of 36.8 mo, the no-blockers group had a mean graft survival of 19.3 mo vs. 72.5 mo for blocker-treated patients. Reinstitution of dialysis occurred less often with calcium channel blockers (17 vs. 42%) or beta blockers (19 vs. 38%) used either individually or together (5 vs. 42%), all. Calcium channel blocker-treated patients had 1/9 the no. of septic deaths, fewer patients had multiple septic episodes, all. Allograft success and patient survivals may be improved and sepsis related events diminished when diabetic renal allograft recipients are treated with calcium channel blocking agents, plus or minus beta blockers. Considerable savings can be accomplished and graft results with these drugs can approach non-diabetic and live-related transplant results.
IT **29122-68-7, Atenolol**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(role of calcium channel blockers in diabetic renal transplant patients: preliminary observations on protection from sepsis)

L7 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1994:401679 HCAPLUS
DOCUMENT NUMBER: 121:1679
TITLE: 5-Hydroxytryptamine causes rate-dependent arrhythmias through 5-HT4 receptors in human atrium: facilitation by chronic .beta.-adrenoceptor blockade
AUTHOR(S): Kaumann, Alberto J.; Sanders, Louise
CORPORATE SOURCE: Addenbrooke's Hosp., Univ. Cambridge, Cambridge, CB2 2QQ, UK
SOURCE: Naunyn-Schmiedeberg's Arch. Pharmacol. (1994), 349(4), 331-7
CODEN: NSAPCC; ISSN: 0028-1298
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have investigated the ability of 5-hydroxytryptamine (5-HT) to elicit arrhythmic contractions in isolated human atrial strips as a function of pacing rate (0.1-2 Hz) using a method recently introduced by the authors and examd. the nature of the 5-HT receptors involved. Right atrial appendage tissue was obtained from 14 patients undergoing cardiac **surgery**. None of the patients had advanced heart failure. 5-HT (0.6-20 .mu.mol/l) induced arrhythmic contractions during pacing in 4/11 atrial strips from 3/4 patients who had not received .beta. blockers and in 21/27 atrial strips from 9/10 patients who had been chronically treated with .beta. blockers (primarily .beta.1-selective). The incidence of arrhythmic contractions evoked by 5-HT did not reach statistical significance in the atrial tissue from the non-.beta. blocked patients but was highly significant in the atrial tissue from the chronically .beta. blocked patients. The arrhythmic contractions usually occurred more frequently at low than at high pacing rates and were obsd. at the physiol. frequency of 1 Hz in 1/4 atrial strips from 1/4 of the non-.beta. blocked patients and 6/11 strips from 5/10 of the .beta. blocked patients. The 5-HT-evoked arrhythmic contractions were obsd. during blockade of .beta.1-adrenoceptors, .beta.2-adrenoceptors and 5-HT3 receptors, ruling out the participation of these receptors. The 5-HT-evoked arrhythmic contractions were totally inhibited within 30 min by the selective 5-HT4 receptor antagonist SB 203186 ((1-piperidinyl)ethyl 1H-indole 3-carboxylate) 100 nmol/L, whereas they persisted in time-matched controls. The blockade of 5-HT-evoked arrhythmic contractions by SB 203186 was surmounted by high concns. (400-1800 .mu.mol/L) of 5-HT. The authors' results demonstrate that 5-HT elicits rate-dependent arrhythmic contractions in isolated human atrium through the 5-HT4 receptor and that they are facilitated on atrial tissue from patients treated with .beta. blockers. The authors' results suggest that endogenous, platelet-derived 5-HT may cause atrial arrhythmias and that exogenous 5-HT4 agonists/partial agonists may be arrhythmogenic.

IT **29122-68-7, Atenolol**
RL: BIOL (Biological study)
(serotonin induction of rate-dependent arrhythmia in human atrium mediation by HT4 receptors facilitation by)

L7 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:589419 HCAPLUS
DOCUMENT NUMBER: 103:189419
TITLE: Effect of the combination of diltiazem and **atenolol** on exercise-induced regional myocardial ischemia in conscious dogs
AUTHOR(S): Matsuzaki, Masunori; Guth, Brian; Tajimi, Tsukasa;

Kemper, W. Scott; Ross, John, Jr.
CORPORATE SOURCE: Sch. Med., Univ. California, San Diego, La Jolla, CA, 92093, USA
SOURCE: Circulation (1985), 72(1), 233-43
CODEN: CIRCAZ; ISSN: 0009-7322
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effect of combination therapy with diltiazem [42399-41-7] and **atenolol** [**29122-68-7**] on the regional myocardial blood flow-function relationship was studied in conscious dogs with chronic coronary artery stenosis. Eighteen days (av.) after **surgery**, resting regional myocardial function and blood flow were normal, but treadmill exercise induced severe myocardial dysfunction in the posterior wall (wall thickening during systole reduced from 25.5%-2.7%, a 90% redn.). Subendocardial blood flow decreased by 68% from the control standing value, whereas subepicardial flow increased. An identical exercise bout was performed 3 h after administration of **atenolol** (1.0 mg/kg, orally) and 15 min after administration of diltiazem (0.3 mg/kg, i.v.). Heart rate during running was lower as were left ventricular peak systolic pressure, end-diastolic pressure, and peak dP/dt. Wall thickening in the control region was not augmented during exercise after **atenolol** and diltiazem. There was less dysfunction in the ischemic region (35% redn.) and the improved performance was accompanied by a substantial increase in subendocardial perfusion. Epicardial flow was unchanged, and the endocardial-epicardial ratio increased. Recovery time for regional wall thickening also improved. The beneficial effects of the combination of **atenolol** and diltiazem in a prepn. of single-vessel chronic coronary stenosis are significantly greater than those of either drug alone.

IT **29122-68-7**
RL: BIOL (Biological study)
(heart function in exercise-induced myocardial ischemia and coronary artery stenosis response to diltiazem combination with)

=> d stat que l9

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L1             1 SEA FILE=REGISTRY ATENOLOL/CN
L3               SEL  L1 1- CHEM :       10 TERMS
L4          3108 SEA FILE=HCAPLUS L3
L5          3108 SEA FILE=HCAPLUS L4 OR ATENOLOL
L6           491 SEA FILE=HCAPLUS L5 AND (CARDIOVASCUL? OR HEART(W)(DISEASE? OR
                 DISORDER?) OR THROMBOSIS OR ANGINA OR DYSRHYTHMIA)
L7             8 SEA FILE=HCAPLUS L6 AND ?SURG?
L8            34 SEA FILE=HCAPLUS (L5(L)(?SURGER? OR ?OPERAT?)) NOT L7
L9            18 SEA FILE=HCAPLUS L8 AND (HEART OR ?CARDIO? OR ?RHYTHMI?)
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=> d l9 ibib abs hitrn

L9 ANSWER 1 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:29536 HCAPLUS
DOCUMENT NUMBER: 132:58973
TITLE: Renal hemodynamic changes during smoking: effects of adrenoreceptor blockade

AUTHOR(S): Benck, U.; Clorius, J. H.; Zuna, I.; Ritz, E.
CORPORATE SOURCE: Department Internal Medicine, Ruperto Carola University, Heidelberg, Germany
SOURCE: Eur. J. Clin. Invest. (1999), 29(12), 1010-1018
CODEN: EJCIB8; ISSN: 0014-2972
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cigarette smoking accelerates progression of renal failure in diabetic and nondiabetic renal disease. Renal hemodynamics during smoking are characterized by a reversible decrease in glomerular filtration rate (GFR) and filtration fraction (FF) accompanied by increased renovascular resistance (RVR), systemic blood pressure, **heart** rate and plasma catecholamine concns. To further assess the role of sympathetic overactivity we compared the effects of different pharmacol. interventions on smoking-induced changes of renal hemodynamics in occasional smokers. In a first series, placebo pretreatment plus smoking was compared to Prazosin pretreatment (3 mg) plus smoking. In a second study, placebo pretreatment plus smoking was compared to **Atenolol** pretreatment (50 mg) plus smoking. Basal blood pressure was significantly lower with Prazosin and **Atenolol**. On placebo, GFR and FF decreased significantly during smoking and RVR increased. With Prazosin pretreatment compared to placebo pretreatment no statistically significant differences for the changes of GFR, FF, RPF and RVR were seen. In contrast, with **Atenolol** pretreatment compared to placebo pretreatment, the smoking-induced changes in active renin, GFR and RVR were significantly smaller. It is suggested that the acute renal hemodynamic effects of smoking are mediated, at least in part, via increased sympathetic activity **operating** mainly through beta-1 adrenergic mechanisms.

=> .

. IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
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"HELP COMMANDS" at an arrow prompt (=>).

=> d l9 ibib abs hitrn 2-18

L9 ANSWER 2 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:180546 HCAPLUS
DOCUMENT NUMBER: 130:261350
TITLE: Effects of antihypertensive single-drug therapy on **heart** rate
AUTHOR(S): Materson, Barry J.; Reda, Domenic J.; Williams, David W.
CORPORATE SOURCE: Department of Medicine, University of Miami, Miami, FL, 33136, USA
SOURCE: Am. J. Hypertens. (1999), 12(1, Pt. 2), 9S-11S
CODEN: AJHYE6; ISSN: 0895-7061
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 6 refs. **Heart** rate increasingly is being recognized either as an independent risk factor for a wide variety of **cardiovascular** disorders or as a surrogate marker for them. We analyzed the changes in **heart** rate assocd. with antihypertensive therapy with six drugs and placebo from the VA **Cooperative** Study on Single-Drug Therapy. These results were published previously (American Journal of Hypertension 1998;11:597-601). This paper provides a summary of the earlier publication with the addn. of three figures not previously published. **Atenolol** had the greatest effect on **heart** rate redn., followed by clonidine and diltiazem-SR. Hydrochlorothiazide and captopril were assocd. with small redns. in **heart** rate over time, whereas prazosin increased **heart** rate. Patients whose blood pressure was controlled by placebo had a 3.1 beats/min redn. of **heart** rate at 2 yr. When the baseline **heart** rate was 65 beats/min or less, all drugs increased the **heart** rate except for **atenolol**, which further reduced it. Although it is clear that each of the six drugs used in our study had a different effect on **heart** rate, we cannot state that drug-induced redn. in **heart** rate per se confers a decrease in **cardiovascular** risk.

L9 ANSWER 3 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:171258 HCAPLUS
DOCUMENT NUMBER: 130:332568
TITLE: Total arterial compliance in ambulatory hypertension during selective .beta.1-adrenergic receptor blockade and angiotensin-converting enzyme inhibition
AUTHOR(S): Soma, Johannes; Aakhus, Svend; Dahl, Ketil; Widero, Tor-Erik; Skjaerpe, Terje
CORPORATE SOURCE: Department of Medicine, Sections of Cardiology, University Hospital of Trondheim, Trondheim, N-7006, Norway
SOURCE: J. Cardiovasc. Pharmacol. (1999), 33(2), 273-279
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aortic root flow and pressure ests. were obtained noninvasively with Doppler **echocardiog**. and calibrated subclavian artery pulse tracing in 30 subjects with ambulatory hypertension in a randomized, crossover study with 4 wk' treatment and washout periods. Total arterial compliance, assessed by use of a three-element Windkessel model of the arterial tree, increased 42% with **atenolol** (50-100 mg once daily), and 7% (p = NS) with captopril (25-50 mg twice daily). **Atenolol** reduced mean arterial pressure by 15%, **heart** rate by 22%, and cardiac output by 14%, and increased acceleration time of aortic root flow by 17% and stroke vol. and ejection time each by 11%. Captopril reduced mean arterial pressure and total peripheral resistance each by 7%. Acceleration time of aortic root flow, ejection time, **heart** rate, stroke vol., and cardiac output were not significantly changed by captopril. We conclude that total arterial compliance, at the **operational** blood pressure, increases during selective .beta.1-adrenergic receptor blockade in subjects with ambulatory hypertension. Although the main mechanism may be a redn. in mean arterial pressure, it should be considered whether reduced **heart** rate may play an addnl. role. The nonsignificant increase in total arterial

compliance during angiotensin-converting enzyme inhibition may primarily be a consequence of a modest redn. of the mean arterial pressure.

L9 ANSWER 4 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:769835 HCAPLUS
DOCUMENT NUMBER: 130:176988
TITLE: Urapidil: a reappraisal of its use in the management of hypertension
AUTHOR(S): Dooley, Mukta; Goa, Karen L.
CORPORATE SOURCE: Adis International Limited, Auckland, N. Z.
SOURCE: Drugs (1998), 56(5), 929-955
CODEN: DRUGAY; ISSN: 0012-6667
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 52 refs. Urapidil is a peripheral postsynaptic .alpha.1-adrenoceptor antagonist with central agonistic action at serotonin 5-HT1A receptors. It reduces blood pressure by decreasing peripheral vascular resistance. Oral urapidil decreases blood pressure in patients with mild to moderate essential hypertension and assocd. risk factors such as hyperlipidemia or type 2 (non-insulin-dependent) diabetes mellitus, with no effect on **heart** rate. The antihypertensive efficacy of urapidil is similar to that of most similar compds. in patients with mild to moderate essential or secondary hypertension and no concomitant risk factors. However, the antihypertensive efficacy of urapidil was lower than that of hydrochlorothiazide in a well-designed trial. Lipid levels and glucose metab. are not adversely affected and may improve with urapidil in patients with lipid or glucose abnormalities. Urapidil can be safely combined with other antihypertensive agents such as hydrochlorothiazide and nifedipine and it improves blood pressure control in previous nonresponders to monotherapy. I.v. urapidil reduces blood pressure in patients with pre-eclampsia or hypertension in pregnancy and in patients with hypertensive crises or peri- or **postoperative** hypertension. The decrease in blood pressure is similar to that after nifedipine, enalaprilat, sodium nitroprusside and dihydralazine, greater than that of ketanserin according to 1 larger study, and greater than that of sublingual nitroglycerin in 1 trial in patients with nonsurgical hypertensive crises and pulmonary edema. However, more patients responded to treatment with urapidil than with enalaprilat or nifedipine. **Heart** rate is less likely to be altered by urapidil than with some similar drugs. Urapidil appears to be well tolerated, with most adverse events being mild and transient. The incidence of adverse events with urapidil is similar to that with prazosin, metoprolol, **atenolol**, sodium nitroprusside and hydrochlorothiazide and less than that with nifedipine and clonidine. Urapidil may not be as well tolerated as captopril and, in 1 study, more urapidil than nitrendipine recipients discontinued treatment because of adverse events. It is concluded that urapidil reduces blood pressure without altering **heart** rate. The oral formulation is an effective choice in patients with hypertension and concomitant dyslipidemia or type 2 diabetes mellitus, in whom the drug does not adversely affect--and may even improve--lipid profiles and glucose metab. The i.v. formulation is effective in controlling various hypertensive crises and hypertension assocd. with pregnancy or **surgery** and is similar to or better than other 1st-line agents used in these conditions. Thus, urapidil may be a useful alternative to currently available antihypertensive agents.

L9 ANSWER 5 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:540284 HCAPLUS
DOCUMENT NUMBER: 129:254887
TITLE: Catechol activation in the vasomotor center upon emergence from anesthesia: specificity
AUTHOR(S): Rentero, Nicolas; Bruandet, Nadine; Viale, Jean Paul; Quintin, L.
CORPORATE SOURCE: Department of Physiology, School of Medicine, Lyon, Fr.
SOURCE: Synapse (N. Y.) (1998), 30(2), 130-139
CODEN: SYNAET; ISSN: 0887-4476
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The rostral ventrolateral medulla (RVLM) controls the vascular system. It may contribute to **postoperative** hypertension obsd. upon emergence from anesthesia. This structure contains adrenergic **cardiovascular** neurons. Therefore, one question was addressed: does a change in RVLM catechol activity occur upon emergence from anesthesia. Halothane-anesthetized, paralyzed rats had their ventilatory, circulatory, and acid-base stability controlled. All pressure points and incisions were infiltrated with local anesthetic. With in vivo electrochem., a catechol signal was recorded in the RVLM in the following circumstances: (1) under stable halothane anesthesia for 120 min (halothane group), (2) during 120 min after halothane discontinuation (saline-emergence group), (3) during 60 min after halothane discontinuation followed by 60 min after halothane readministration (readministration group), (4) emergence in rats treated with **atenolol** and nitroprusside to hold blood pressure as close as possible to baseline, (5) emergence after morphine 1 mg.kg-1 i.v., (6) emergence after decerebration, and (7) emergence upon recording in the mid-brain dopaminergic A10 area. Stable halothane anesthesia (n = 6) led to no change in mean arterial pressure (MAP), **heart** rate (HR), and catechol signal (CAOC). During emergence from anesthesia (n = 6), MAP, HR, and catechol signal increased and did not return to baseline. By contrast, a return of MAP, HR, and catechol signal to baseline was obsd. upon readministration of halothane (n = 6). Whereas blood pressure and **heart** rate were maintained as closely as possible to baseline, a large catechol activation (n = 5) was obsd. upon emergence from anesthesia. A catechol activation from a lowered baseline was obsd. upon emergence following morphine administration (n = 5). A minor circulatory activation without RVLM catechol activation was obsd. upon emergence following decerebration (n = 5). Recordings in the A10 area revealed no increase in the catechol signal following emergence (n = 5). Adrenergic RVLM neurons appear to be responsive upon emergence from anesthesia, possibly being activated by suprapontine afferents impinging on the RVLM.

L9 ANSWER 6 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:90695 HCAPLUS
DOCUMENT NUMBER: 128:212995
TITLE: Relations between fasting serum insulin, glucose, and dehydroepiandrosterone-sulfate concentrations in obese patients with hypertension: short-term effects of antihypertensive drugs
AUTHOR(S): Fuenmayor, Nery T.; Moreira, Elizabeth; de los Rios,

Victoria; Cevallos, Jose L.; Cubeddu, Luigi X.
CORPORATE SOURCE: Nephrology Div., Hypertension Unit, Hospital Miguel Perez Carreno, Caracas, Venez.
SOURCE: J. Cardiovasc. Pharmacol. (1997), 30(4), 523-527
CODEN: JCPCDT; ISSN: 0160-2446
PUBLISHER: Lippincott-Raven Publishers
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A randomized, single-blind, placebo-controlled study was conducted in 82 obese patients with mild to moderate essential hypertension, to det. the incidence of hyperinsulinemia, the relations between fasting insulin and dehydroepiandrosterone-sulfate (DHEA-S) levels, and the short-term effects of antihypertensives on DHEA-S and insulin serum concns. Increased insulin/glucose ratios (IGR) suggestive of insulin resistance were found in half of our patients. Hyperinsulinemic and normoinsulinemic obese patients with hypertension had comparable fasting glucose and DHEA-S concns. and comparable blood pressure (BP) levels. Thus no relations were found between fasting insulin and DHEA-S levels. Fasting hyperinsulinemia was found in only half of the obese subjects with hypertension, suggesting that not all obese patients with hypertension are at the same high **cardiovascular** risk. Short-term treatment with captopril, prazosin, verapamil, **atenolol**, or hydrochlorothiazide (HCTZ) reduced BP; greater BP redn. was obsd. with drugs with vasodilatory effects. Captopril, prazosin, and verapamil reduced fasting insulin levels, whereas **atenolol** and hydrochlorothiazide did not. The former drugs reduced fasting insulin levels that were either within normal limits or in the hyperinsulinemic range. None of the drug treatments produced significant increases in serum DHEA-S concns., although some of them considerably reduced fasting insulin levels. No relations between insulin and DHEA-S levels were obsd. either at baseline or at the end of the antihypertensive treatment. The BP redn. resulting from the peripheral vasodilation may explain the insulin-reducing action of captopril, verapamil, and prazosin. These results further emphasize the large heterogeneity present in the pathophysiol. mechanisms **operating** in obesity and hypertension.

L9 ANSWER 7 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:399952 HCAPLUS
DOCUMENT NUMBER: 125:104128
TITLE: Determination of sotalol in human cardiac tissue by high-performance liquid chromatography
AUTHOR(S): Laeer, Stephanie; Neumann, Joachim; Scholz, Hasso; Uebeler, Phaslia; Zimmermann, Norbert
CORPORATE SOURCE: Abteilung Allgemeine Pharmakologie, Universitaets-Krankenhaus Eppendorf, Martinistrasse 52, Hamburg, 20246, Germany
SOURCE: J. Chromatogr., B: Biomed. Appl. (1996), 681(2), 291-298
CODEN: JCBBEP; ISSN: 0378-4347
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A sensitive and quant. reversed-phase HPLC method for the anal. of DL-sotalol in human atria, ventricles, blood and plasma was developed. Sotalol was detd. in about 100 mg of human right atria, left ventricles, and in 500 .mu.L of blood and plasma samples of patients undergoing coronary bypass **surgery** or **heart** transplantation.

Patients were taking 80-160 mg of sotalol as an **antiarrhythmic** agent. **Atenolol** was used as an internal std. certifying high precision of measurement. Sotalol blood and plasma concns. correlated linearly to the obtained signals from 26.5 ng/mL to 2.12 .mu.g/mL. Sotalol tissue concns. showed linearity between 0.27 ng/mg and 10.6 ng/mg wet wt. The limit of quantitation was 0.27 ng/mg at a signal-to-noise ratio of 10. Sotalol was extd. from homogenized tissue with a buffer soln. (pH 9) and the remaining pellet was extd. with methanol. The methanol ext. was evapd. under nitrogen and reconstituted in buffer (pH 3). The whole ext. was cleaned by solid-phase column extn., eluted with methanol, evapd. again, reconstituted in the mobile phase (acetonitrile-15 mM potassium phosphate buffer pH 3, 17:83, vol./vol.) and injected onto the HPLC column (Spherisorb C6 column, 5 .mu.m, 150.times.4.6 mm I.D.). For the detection of sotalol, the UV wavelength was set to 230 nm. Recoveries of sotalol and **atenolol** in atria and ventricles were 65.6 and 75.0%, resp. Intra- and inter-assay coeffs. of variation for tissue concns. were 3.38 and 6.14%, resp. Intra- and inter-assay accuracy for detd. tissue sotalol concns. were 94.9 and 99.6%, resp.

L9 ANSWER 8 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:645951 HCAPLUS
DOCUMENT NUMBER: 123:102332
TITLE: Effect of prolonged beta-adrenergic blockade induced by atenolol on left ventricular remodeling after acute myocardial infarction in the rat
AUTHOR(S): Shimada, Ken-ei; Nishikimi, Toshio; Kawarabayashi, Takahiko; Takeuchi, Kazuhide; Takeda, Tadanao
CORPORATE SOURCE: Medical School, Osaka City University, Suita, 565, Japan
SOURCE: Jpn. Heart J. (1995), 36(1), 81-9
CODEN: JHEJAR; ISSN: 0021-4868
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Beta-adrenergic receptor blockade reduces the mortality rate after acute myocardial infarction (AMI) in humans. However, the effects of beta blockade on left ventricular remodeling remain unknown. Therefore, in the present study the effect of prolonged beta-adrenergic receptor blockade with **atenolol** on left ventricular remodeling following AMI was investigated in rats. Myocardial infarction (MI) was produced in Wistar-Kyoto rats by ligating the coronary artery. Four groups of rats were studied: sham-**operated** (n = 10); **atenolol** (1 g/L in drinking water) treated sham-**operated** (n = 8); untreated MI (n = 11); **atenolol** treated MI (n = 10). Hemodynamic measurements were made about 3 wk after the **operation**. Infarct size was similar in treated and untreated MI rats (31.2 .+-. 2.5% cf. 33.5 .+-. 2.0%). MI rats were characterized by increases in left ventricular end-diastolic pressure (LVEDP), right atrial pressure (RAP), right ventricular systolic pressure (RVSP), and left ventricular end-diastolic vol. index (LVEDVI), as compared with sham-**operated** rats. In sham-**operated** rats, prolonged beta-adrenergic receptor blockade produced only a reduced HR. **Atenolol**-treated MI rats had a significantly higher LVEDP, RAP and LVEDVI than did rats with untreated MI. Prolonged beta-adrenergic receptor blockade with **atenolol** appeared to promote left ventricular remodeling after AMI. Thus, the treatment of AMI with beta-adrenergic receptor blockade in the clin. setting should be evaluated with respect to ventricular remodeling during

prolonged therapy.

L9 ANSWER 9 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:611935 HCAPLUS
DOCUMENT NUMBER: 123:53410
TITLE: Coronary microvascular .beta.-adrenoceptor subtypes and crystalloid **cardioplegia**
AUTHOR(S): Wang, Steven Y.; Friedman, Menachem; Johnson, Robert G.; Sellke, Frank W.
CORPORATE SOURCE: Harvard Medical School, Beth Israel Hospital, Boston, MA, 02215, USA
SOURCE: Resist. Arteries (1994), 357-64. Editor(s): Halpern, William. Humana: Totowa, N. J.
CODEN: 61KCA3
DOCUMENT TYPE: Conference
LANGUAGE: English
AB To examine the effect of crystalloid **cardioplegia** on the different .beta.-adrenoceptor subtypes in the coronary microcirculation, we compared microvascular responses before and after **cardioplegic** arrest. Pigs were placed on **cardiopulmonary** bypass and hearts were arrested with cold hyperkalemic crystalloid soln. After 1 h, hearts were reperfused for 1 h. In vitro coronary arteriolar responses to isoproterenol and the adenylate cyclase activator forskolin were studied in a pressurized, no-flow state with a video-microscopy. After contraction of vessels by 25% to 50% of the baseline diam., drugs were applied extraluminally. Isoproterenol-induced relaxation of vessels in the presence of ICI-118,551 (.beta.2-blocker) was significantly less than that of vessels in the presence of **atenolol** (.beta.1-blocker). Thus, coronary microvascular relaxation to isoproterenol is primarily due to .beta.2-adrenoceptor stimulation. Crystalloid **cardioplegia** reduced relaxations to .beta.1- or .beta.2-stimulation and to forskolin. Following reperfusion, the relaxation responses to forskolin and .beta.1- or .beta.2-adrenergic stimulation were completely restored. **Cardioplegic** arrest and reperfusion blunted endothelium-dependent relaxation to ADP, whereas endothelium-independent relaxation to sodium nitroprusside was not affected. Therefore, the present study demonstrates that crystalloid **cardioplegia** reduces the .beta.1- and .beta.2-adrenoceptor-mediated and cAMP-dependent relaxation in the coronary microcirculation. The **cardioplegia**-induced alteration in the coronary microvascular .beta.-adrenergic mechanism may be responsible for episodic coronary spasm and altered myocardial perfusion following cardiac **surgery**.

L9 ANSWER 10 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:595386 HCAPLUS
DOCUMENT NUMBER: 119:195386
TITLE: In vivo regulation of human cardiac .beta.-adrenoceptors by a partial agonist as compared with a full antagonist: Selective differences in coupling to adenylate cyclase
AUTHOR(S): Arnold, Ian R.; Mistry, Rajendra; Barnett, David B.
CORPORATE SOURCE: Dep. Clin. Pharmacol., Leicester R. Infirm., Leicester, LE2 7LX, UK
SOURCE: J. Cardiovasc. Pharmacol. (1993), 22(3), 481-7
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal

LANGUAGE: English
AB Chronic therapy with the .beta.1-selective adrenoceptor partial agonist xamoterol is not assocd. with the tolerance obsd. with other .beta.-adrenoceptor agonist. A possible explanation is that xamoterol therapy does not desensitize human cardiac .beta.-adrenoceptors in vivo. .beta.-Adrenoceptor d. and adenylate cyclase activities were detd. in right atrial appendages obtained from 40 patients randomized in a double-blind fashion to receive either xamoterol or **atenolol** for at least 5 wk before coronary artery bypass **surgery**. There was no significant difference in total or subtype .beta.-adrenoceptor densities, but basal and isoproterenol stimulated adenylate cyclase activity were significantly greater in the **atenolol**-treated group, as was the intrinsic activity of the .beta.2-adrenoceptor partial agonist procaterol, suggesting that chronic therapy with xamoterol does not downregulate human cardiac .beta.-adrenoceptors in vivo. Coupling of .beta.-adrenoceptors to adenylate cyclase, predominantly mediated by the .beta.2 subtype, is enhanced, however, after therapy with **atenolol** relative to therapy with xamoterol.

L9 ANSWER 11 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1993:573951 HCAPLUS
DOCUMENT NUMBER: 119:173951
TITLE: Administration of nebivolol after coronary artery bypass in patients with altered left ventricular function
AUTHOR(S): Goldstein, Marcelo; Vincent, Jean Louis; De Smet, Jean Marie; Barvais, Luc; Van Nueten, Luc; Scheijgrond, Henk; d'Hollander, Alain; Leclerc, Jean Louis; Kahn, Robert J.
CORPORATE SOURCE: Dep. Intensive Care, Erasme Univ., Brussels, Belg.
SOURCE: J. Cardiovasc. Pharmacol. (1993), 22(2), 253-8
CODEN: JCPCDT; ISSN: 0160-2446
DOCUMENT TYPE: Journal
LANGUAGE: English
AB This prospective, double-blind study used invasive monitoring and echo-Doppler techniques to compare the hemodynamic effects of nebivolol, a new .beta.1-selective .beta.-blocking agent with those of **atenolol** in patients recovering from coronary artery bypass grafting **surgery**. Five milligrams nebivolol and 50 mg **atenolol** equally decreased **heart** rate (HR) and blood pressure (BP) but, nebivolol, in contrast to **atenolol**, caused no decrease in stroke index (SI), cardiac index (CI), and right ventricular ejection fraction (RVEF). These differences appeared to be related in part to different peripheral effects of the two agents because nebivolol administration was assocd. with a redn. in systemic vascular resistance (SVR). After .ltoreq.10 days of treatment, acceleration of aortic flow velocity increased and isovolumic relaxation time decreased with nebivolol but not with **atenolol** treatment. Both drugs were equally well tolerated. Therefore, nebivolol shares most of its effects with classical .beta.1-blockers but is devoid of the potentially harmful effects on cardiac output (CO) and peripheral resistance.

L9 ANSWER 12 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1992:526188 HCAPLUS
DOCUMENT NUMBER: 117:126188
TITLE: Action of ciguatoxin on human atrial trabeculae

AUTHOR(S): Lewis, RIchard J.; Hoy, Ashley W. Wong; McGiffin, David C.
CORPORATE SOURCE: South. Fish. Cent., QDPI, Deception Bay, 4508, Australia
SOURCE: Toxicon (1992), 30(8), 907-14
CODEN: TOXIA6; ISSN: 0041-0101
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ciguatoxin-1 caused a large, sustained and concn.-dependent pos. inotropy in human atrial trabeculae that were obtained during coronary artery bypass **surgery** from otherwise healthy hearts. **Atenolol** (a .beta.1-adrenoceptor selective antagonist without local anesthetic-type activity) or low concns. of tetrodotoxin abolished the pos. inotropy caused by ciguatoxin-1, indicating that ciguatoxin-1 stimulated neural elements present in this tissue to release noradrenaline. The pos. inotropic action of ciguatoxin-1 did not stem from a significant direct action on myocardial voltage-dependent sodium channels, nor did it stem from significant .alpha.1- or .beta.2-adrenoceptor stimulation. Ciguatoxin-1 caused pos. inotropy in prepns. stimulated at between 0.02 and 2.0 Hz. Mannitol, currently the treatment of choice for ciguatera, did not significantly reverse the pos. inotropy induced by ciguatoxin-1 in human atrial trabeculae.

L9 ANSWER 13 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1991:624499 HCAPLUS
DOCUMENT NUMBER: 115:224499
TITLE: Specific non-.beta.-adrenergic binding sites for 125I-iodocyanopindolol in myocardial membrane preparations: a comparative study between human, rat, and porcine hearts
AUTHOR(S): Bjoernerheim, Reidar; Golf, Svein; Hansson, Vidar
CORPORATE SOURCE: Med. Dep. B, Rikshosp., Oslo, Norway
SOURCE: Cardiovasc. Res. (1991), 25(9), 764-73
CODEN: CVREAU; ISSN: 0008-6363
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The aim was to investigate obsd. differences in .beta.-adrenergic and apparent non-.beta.-adrenergic binding of (-)[125I]-iodocyanopindolol (125I-ICYP). Binding parameters for several .beta.-adrenergic agonists and antagonists were examd. in radioligand binding assay, using 125I-ICYP as radioligand, in membranes prepd. from myocardial tissue. Human right auricular myocardium was obtained from patients undergoing open **heart surgery**. Ventricular myocardium was from Norwegian landrace pigs and Wistar rats. Specific binding of 125I-ICYP was obsd. This was only partially competed for with high affinity by isoprenaline, noradrenaline, adrenaline, and **atenolol**. Considerable interspecies variations in the magnitude of specific non-.beta.-adrenergic (NBA) binding of 125I-ICYP were shown. The equil. const. of dissocn. (Kd) of specific NBA binding sites for 125I-ICYP was 0.3-0.4 nM, and the binding capacities were 20, 106, and 192 fmol/mg protein in rat, human, and porcine myocardium, resp. The NBA sites were heat sensitive and destroyed by trypsin. Assocn. to NBA sites occurred more rapidly than to .beta.-adrenoceptors. Dissocn. of bound 125II-ICYP from NBA sites and .beta.-adrenoceptors at 30.degree. revealed 1st-order kinetics with t1/2 of 19 min from NBA, as compared to 120 min from .beta.-adrenoceptors. In all 3 species the ligand specificity for NBA

sites was very similar and various adrenergic agonists and antagonists competed with 125I-ICYP binding with the following potencies: timolol > propranolol > ICI 118 551 > pindolol > Sandoz 204 545 > terbutaline > noradrenaline and adrenaline .mchgt. isoprenaline and **atenolol**. Of agonists and antagonists for other receptor systems, only the serotoninergic 5-HT2 antagonist ritanserin could displace 125I-ICYP from the NBA sites with relatively high affinity. 125I-ICYP and several .beta.-adrenoceptor antagonists interact specifically with receptor-like proteins other than B-adrenoceptors, and remarkable interspecies difference in the levels of myocardial NBA sites was obsd.

L9 ANSWER 14 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1989:490998 HCAPLUS
DOCUMENT NUMBER: 111:90998
TITLE: A comparison of the effects of adrenaline and noradrenaline on human **heart**: the role of .beta.1- and .beta.2-adrenoceptors in the stimulation of adenylate cyclase and contractile force
AUTHOR(S): Kaumann, A. J.; Hall, J. A.; Murray, K. J.; Wells, F. C.; Brown, M. J.
CORPORATE SOURCE: Smith Kline and French Res. Ltd., Welwyn/Hertfordshire, UK
SOURCE: Eur. Heart J. (1989), 10(Suppl. B), 29-37
CODEN: EHJODF; ISSN: 0195-668X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The stimulant effects of adrenaline and noradrenaline on contractile force and adenylate cyclase, mediated through .beta.1- and .beta.2-adrenoceptors, are analyzed in isolated atrial and ventricular myocardium of man. The tissues were obtained from patients without advanced **heart** failure undergoing **heart surgery**. Usually, both adrenaline and noradrenaline stimulated adenylate cyclase predominantly through ventricular and atrial .beta.2-adrenoceptors. Because the relative d. of .beta.2-adrenoceptors is usually smaller than that of .beta.1-adrenoceptors, stimulation of one .beta.2-adrenoceptor leads to the prodn. of up to 10 times more cAMP mols. than does stimulation of one .beta.1-adrenoceptor. Adrenaline and noradrenaline maximally enhance contractile force through both atrial and ventricular .beta.1-adrenoceptors. Adrenaline can also maximally enhance contractile force through atrial .beta.2-adrenoceptors. In the ventricle, adrenaline increases force via .beta.2-adrenoceptors by up to 60% of its maximal .beta.1 response. Noradrenaline can increase atrial and ventricular contractile force through .beta.2-adrenoceptors but only at high concns. Unexpectedly, in atria from patients treated with the .beta.1-selective antagonist **atenolol**, contractile responses to adrenaline are markedly and selectively augmented through activation of .beta.2-adrenoceptors. In atria from **atenolol**-treated patients equi-inotropic concns. of adrenaline and noradrenaline acting through .beta.2- and .beta.1-adrenoceptors, resp., cause similar increases of cAMP and of cAMP-dependent protein kinase activity.

L9 ANSWER 15 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1989:471517 HCAPLUS
DOCUMENT NUMBER: 111:71517
TITLE: **Cardiovascular** effects of the N-methyl-D-aspartate receptor antagonist MK-801 in

conscious rats

AUTHOR(S): Lewis, Stephen J.; Barres, Christian; Jacob, Howard J.; Ohta, Hisashi; Brody, Michael J.

CORPORATE SOURCE: Coll. Med., Univ. Iowa, Iowa City, IA, 52242, USA

SOURCE: Hypertension (Dallas) (1989), 13(6, Pt. 2), 759-65
CODEN: HPRTDN; ISSN: 0194-911X

DOCUMENT TYPE: Journal

LANGUAGE: English

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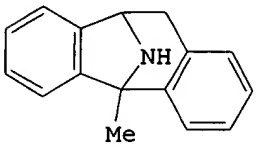

I

AB Central excitatory amino acid pathways using N-methyl-D-aspartate receptors are apparently involved in the regulation of the **cardiovascular** system. To test the hypothesis that these pathways are tonically involved in the maintenance of or the baroreceptor reflex regulation of **cardiovascular** function, the effects of i.v. injection of the centrally acting, noncompetitive N-methyl-D-aspartate receptor antagonist (+)-5-methyl-10,11-dihydro-5H-dibenzo[a,d]cyclohepten-5,10-imine (MK-801) (I) were examd. on the mean arterial pressure, **heart** rate, renal sympathetic nerve activity, and behavior of conscious, freely moving sham-**operated** and sinoaortic baroreceptor-denervated rats. Administration of MK-801 produced, within 5 min, dose-dependent elevations in mean arterial pressure, **heart** rate, and renal sympathetic nerve activity that were sustained for 0.5-2.5 h. For an equiv. dose, MK-801 produced approx. twice the peak changes in mean arterial pressure and **heart** rate in the sinoaortic baroreceptor-denervated rats compared with the sham-**operated** rats. Pretreatment with the ganglion blocker chlorisondamine markedly attenuated the hypertension and tachycardia in the sham-**operated** and sinoaortic baroreceptor-denervated rats, pretreatment with the .alpha.1-adrenergic receptor antagonist prazosin virtually abolished the hypertension, and pretreatment with the .beta.1-adrenergic receptor antagonist **atenolol** markedly reduced the tachycardia. MK-801 also produced stereotypic behaviors and ataxis in the sham-**operated** and sinoaortic baroreceptor-denervated rats; however, qual. and quant. similar changes in behavior were induced in the latter by doses .apprx.20% of those required in the sham-**operated** rats. Thus, the MK-801-induced hypertension and tachycardia appear to result largely from centrally mediated sympathoexcitatory actions, rather than only by inhibition of the baroreceptor reflex. The **cardiovascular** changes produced by MK-801 may, in part, result from the behavioral excitation, and tonically active excitatory amino acid pathways using N-methyl-D-aspartate receptors appear to be involved in the regulation of autonomic function.

L9 ANSWER 16 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1985:147860 HCAPLUS
DOCUMENT NUMBER: 102:147860

TITLE: Kinetic determination of selenium in the blood and organs of rats with experimental myocardial infarction
AUTHOR(S): Kudrin, A. N.; Krasnyuk, I. I.; Efremenko, O. A.
CORPORATE SOURCE: I Mosk. Med. Inst., Moscow, USSR
SOURCE: Farmatsiya (Moscow) (1985), 34(1), 25-9
CODEN: FRMTAL; ISSN: 0367-3014
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB Myocardial infarction (**heart** occlusion) in male rats decreased blood Se (0.34 vs. 0.40 .mu.g/mL) and increased Se content at the infarct site (2.07 vs. 1.54 .mu.g/g). Se supplements (as Na2SeO3; 30 .mu.g/kg for 7 days before infarct) increased the myocardial Se levels (2.71 .mu.g/g in infarct zone and 2.03 in noninfarcted zone) and normalized blood Se. When Na2SeO3 supplements were accompanied by i.v. **atenolol** [**29122-68-7**], a .beta.-adrenergic blocker, at 10 mg/kg i.v. 10 min before infarct **operation** and 6 h later, myocardial Se levels were even higher (3.65 and 2.46 .mu.g/g, resp.).

L9 ANSWER 17 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1982:504152 HCAPLUS
DOCUMENT NUMBER: 97:104152
TITLE: Elevated plasma noradrenaline in response to .beta.-adrenoceptor stimulation in man
AUTHOR(S): Vincent, H. H.; Manin't Veld, A. J.; Boomsma, F.; Wenting, G. J.; Schalekamp, M. A. D. H.
CORPORATE SOURCE: Dep. Intern. Med., Erasmus Univ., Rotterdam, Neth.
SOURCE: Br. J. Clin. Pharmacol. (1982), 13(5), 717-21
CODEN: BCPHBM; ISSN: 0306-5251
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Dose-dependent increments of plasma noradrenaline [51-41-2] were obsd. during graded infusions of (.+-.)isoprenaline [149-53-1] (3.5-35 ng/kg/min, i.v.) in 7 normal subjects and in 10 subjects with borderline hypertension. At the highest dose of isoprenaline, noradrenaline rose by 166 pg/mL in normals and by 169 pg/mL in hypertensives. In the subjects with borderline hypertension, isoprenaline infusions were repeated after 7 days of treatment with (.+-.)propranolol [13013-17-7] (320 mg/day, divided into 4 doses) and subsequently after 7 days of treatment with (.+-.)**atenolol** [**60966-51-0**] (100 mg/day) 2-3 h after the morning dose of .beta.-adrenoceptor blocker. The dose-response curve for plasma noradrenaline was shifted to higher doses of isoprenaline by a factor of 4 by **atenolol** and the **heart** rate response was similarly shifted. The **heart** rate response was shifted by a factor of 16 by propranolol, but plasma noradrenaline did not change after isoprenaline under propranolol treatment, even when isoprenaline was given at doses high enough to induce increments of **heart** rate similar to those without .beta.-adrenoceptor blocker treatment. In the subjects with borderline hypertension mean and diastolic intra-arterial pressures fell at the highest dose of isoprenaline by 9 and 13 mm Hg resp. These effects were antagonized by propranolol and not by **atenolol**. The obsd. rise in plasma noradrenaline after isoprenaline might have been caused by baroreflex-stimulation of central sympathetic outflow. The isoprenaline-induced decrease in mean arterial pressure, however, was small. Moreover pulse pressure rose and this tends to suppress rather than stimulate baroreflex-mediated sympathetic activity. Activation of presynaptic .beta.-adrenoceptors, allegedly of the .beta.2-subtype, is

known to facilitate noradrenaline release upon nerve stimulation of isolated tissues. Apparently, such a facilitatory mechanism is also **operative** in intact man.

L9 ANSWER 18 OF 18 HCAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1982:210743 HCAPLUS
DOCUMENT NUMBER: 96:210743
TITLE: Beta-blocker therapy during general anesthesia. Experimental and clinical studies
AUTHOR(S): Marquort, H.
CORPORATE SOURCE: Zent. Anaesthesieabt., Univ. Kiel, Kiel, D-2300, Fed. Rep. Ger.
SOURCE: Anaesthesiol. Intensivmed. (Berlin) (1981), 141, 54-9
CODEN: ANIMD2; ISSN: 0171-1814
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Based on exptl. and clin. studies, intraoperative acute therapy with .beta.-sympatholytics, which have intrinsic activity, such as pindolol [13523-86-9] during anesthesia is recommended.
IT **29122-68-7**
RL: BIOL (Biological study)
(**heart** contraction response to anesthetics and, during **surgery** in humans)

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DICTIONARY FILE UPDATES: 17 FEB 2000 HIGHEST RN 256353-85-2

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L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2000 ACS
RN 29122-68-7 REGISTRY
CN Benzeneacetamide, 4-[2-hydroxy-3-[(1-methylethyl)amino]propoxy]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Acetamide, 2-[p-[2-hydroxy-3-(isopropylamino)propoxy]phenyl]- (8CI)
OTHER NAMES:
CN (.+-.)-Atenolol
CN (RS)-Atenolol
CN **Atenolol**
CN DL-Atenolol
CN dl-Atenolol
CN Duraatenolol

CN ICI 66082
CN Tenormin
FS 3D CONCORD
DR 106020-65-9, 60966-51-0
MF C14 H22 N2 O3
CI COM
LC STN Files: AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM, DDFU, DRUGPAT, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PHAR, PROMT, RTECS*, SPECINFO, TOXLINE, TOXLIT, USAN, USPATFULL, VETU
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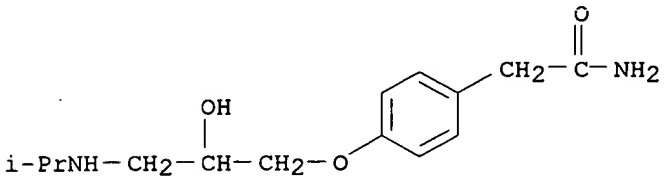

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12 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1978 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:87682

REFERENCE 2: 132:87676

REFERENCE 3: 132:83791

REFERENCE 4: 132:83650

REFERENCE 5: 132:73458

REFERENCE 6: 132:73218

REFERENCE 7: 132:69413

REFERENCE 8: 132:59091

REFERENCE 9: 132:58973

REFERENCE 10: 132:44724

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